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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,418	01/23/2006	Paolo Monaci	ITR0065YP	2202

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MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
ALLEN, MARIANNE P	
ART UNIT	PAPER NUMBER
1647	
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07/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,418	MONACI ET AL.	
	Examiner	Art Unit	
	Marianne P. Allen	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-10 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-10 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5, 11, and 13-24 have been cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 6 has been amended to recite "wherein the HER2ECDTM protein comprises only the extracellular and transmembrane domains of the human HER2 protein." No basis is seen for the limitation "comprises only." The specification does not appear to exclude other portions of the human HER2 protein and the use of comprising in claim 6, line 2, further indicates open language. If applicant intended to claim a synthetic nucleic acid molecule **consisting of** a sequence of nucleotides that encodes SEQ ID NO: 14, this language does not make that clear. If applicant intended something else, it cannot be determined from the specification what was intended. The use of open language ("comprising") and exclusionary language ("only") to describe the claimed synthetic nucleic acid molecules does not appear to have been contemplated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant application is a 371 application of PCT/EP04/08234 filed 7/20/04. It claims priority to provisional application 60/489,237 filed 7/21/03. Benefit to provisional application 60/489,237 is denied and the effective filing date of the instant application is 7/20/04. There is no basis in the provisional application for truncated HER2ECDTM as recited in the claims.

Claims 6-10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheever et al. (U.S. Patent No. 5,69,445) in view of Morris et al. (WO 2004/041065), Foy et al. (2001), Ikemura et al. (1985), and Nakamura et al. (1999).

Cheever et al. (U.S. Patent No. 5,869,445) discloses amino acid sequence SEQ ID NO: 2 which contains the instant SEQ ID NO: 14. Cheever et al. also discloses SEQ ID NO: 1 which

encodes this protein. At column 9, lines 43-51, Cheever et al. discloses modifying the nucleic acid sequence to employ codon bias for recombinant production of the protein in a desired host. Vectors, hosts, and methods of production are disclosed. Cheever et al. discloses various peptide fragments of Her2/neu that would be useful but does not specifically disclose a peptide that has only the extracellular and transmembrane domain.

Morris et al. discloses non-signaling HER-2/neu antigens that lack the cytoplasmic or intracellular domain. Truncated proteins having the transmembrane and extracellular domains are disclosed. The desirability of the human HER-2/neu sequence is disclosed. Codon optimization is disclosed. Administration to humans for vaccine purposes is disclosed. See at least abstract, claims (in particular claims 13, 14, 27, and 28), and pages 3-5 and 48. Morris et al. was published 21 May 2004 and is valid prior art against the instant claims.

Foy et al. (2001) discloses the value of human DNA vaccines for Her2/neu. Thus, it would have been obvious to use human codons for the truncated sequence of Morris et al. as further suggested by Cheever et al. Ikemura et al. (1985) and Nakamura (1999) demonstrate that codon usage in different species would have been well known to those of ordinary skill in the art. The well known purpose of codon optimization would have been to achieve high level expression. While the art does not teach the specific sequence of SEQ ID NO: 9 (see claim 7), all codon optimized sequences would have been obvious. The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results. The skilled artisan would have had reason to try this methodology with the reasonable expectation of success.

Applicant's arguments regarding unpredictability are unpersuasive. It would have been routine in the art at the time of the invention for one of ordinary skill to produce a codon optimized sequence for recombinant production in a variety of hosts. The prior art as a whole indicates that there would have been an expectation of success that a codon optimized sequence would have resulted in improved production. Absolute predictability is not required. Applicant has cited Kim et al., Alexeyev et al., and Coulombe et al. to support their contention of unpredictability. However, these references demonstrate the expectation by those of ordinary skill in the art that improved production will result. They also manipulated other features concerning expression (promoters, vectors, etc.) Note that using human codons in a human EPO sequence (Kim et al.) did provide significantly higher expression.

It is noted that claims 6 and 10 require codon optimization for high level expression. This is suggested by the prior art. The claims do not require a particular level of expression. The claims are not directed to the very best codon sequence (a single, particular sequence) that provides the highest expression under a particular set of conditions or a particular optimized sequence that provides unexpectedly higher expression (i.e. orders of magnitude different than other sequences when compared). If this were so, the claims would be duplicative and redundant as they would all be directed to one specific sequence rather than embracing multiple sequences as they are presently written. The specification does not disclose any sequence as being the very best codon sequence for expression in human cells or as having unexpectedly higher expression when compared with other optimized sequences. Applicant's arguments concerning Figure 8 and Example 14 are not persuasive. This is not a comparision between codon optimized and naturally occurring sequences. It is a comparison between two codon

optimized sequences, a full length sequence and a truncated sequence. It does not establish any unexpected results for the codon optimized sequence. Improved expression is expected. The biological activity is not attributable to the codon optimization but rather the truncation. The prior art suggests codon optimization of the truncated sequence. The intended target is a human. Optimizing with human codons in a human protein for expression in a human host would have been obvious and suggested by the prior art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 571-272-0712. The examiner can normally be reached on Monday-Friday, 5:30 am - 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/
Primary Examiner, Art Unit 1647

mpa